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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	30

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/327,750	SATO, TAKA-AKI	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the c ver sheet with the c rresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *29,55,56 and 131-146* is/are pending in the application.

4a) Of the above claim(s) *29,55,56 and 131-133* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *134-146* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The request filed on 9/27/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/327,750 is acceptable and a CPA has been established. An action on the CPA follows.

1. Formal Matters

A. Amendment F, filed 9/27/02, has been entered into the record.

B. The Raw Sequence Listing, filed 1/6/03, has been entered into the record.

C. Amendment G, filed 12/2/02, has been entered into the record.

D. Claims 1-4, 8-23, 29, 55, 56 and 131-133 were pending in the application. Claims 29, 55, 56, 131 and 133 were withdrawn from consideration as being drawn to a non-elected invention. In Amendment F, Applicants canceled claims 1-4, 8-23 and 132 and added new claims 134-146. Therefore, claims 29, 55, 56 and 131-146 are pending and claims 134-146 are the subject of this Office Action.

E. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Specification

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title is drawn to genes, proteins and methods of using these proteins. However, the claims are drawn toward screening a p75 neurotropin receptor and NADE complex for modulators of apoptosis.

B. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. **It is important that the abstract not exceed 150 words in length** since the space provided for the abstract on the computer tape used by the printer is limited. The form and **legal phraseology often used in patent claims, such as "means" and "said," should be avoided.** The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

C. The specification is objected to since it is not clear whether or not the NADE of SEQ ID NO:12 or 13 of the present invention is identical to that of the known protein, HGR74. The specification makes numerous references that the NADE of the present invention is the known HGR74 protein (pages 6-8 and the Brief Description of Figure 1A). However, the specification also discloses that NADE is only 92.8% *homologous* to HGR74 (page 53, lines 20-25). Furthermore, SEQ ID NO:12 is a mouse protein whereas HGR74 is a human protein. The NADE of the present invention was discloses as being 124 residues. This is consistent with the mouse protein of SEQ ID NO:12. SEQ ID NO:13 of the present invention is a human protein. However, it is only 111 residues; therefore, inconsistent with the teachings of the specification. Clarification of this issue, and amendment of the specification, is required.

4. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 134-146 are rejected under 35 USC 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. Applicants have shown that NADE interacts with p75 in an NGF-dependent manner and also interacts with the cell death domain (page 55, lines 8-16 of the specification; Figure 2). Figures 3A-3C and page 55, line 30 – page 56, line 5 shows that apoptosis only occurs when both p75 and NADE are expressed together. However, as cited by the previous Examiner on page 5 of the Office Action dated 3/27/02, Bunone et al. (Oncogene 14:1463-1470, 1997 – Abstract) teaches that p75 *could* (emphasis added) activate the cell death program (i.e. apoptosis) by itself. Therefore, NADE, nor any other cell death executor, does not appear to be required for apoptosis. Due to these conflicting results, the Examiner is concerned that, though p75 may have a utility, NADE, or the NADE-p75 complex, may not. Applicants also disclose on page 57, lines 1-8 of the specification that NADE itself suppresses NF-kB activity which may lead to apoptosis, but that this is not cooperative with coexpression with p75, to which the claims are drawn. Therefore, The Examiner requests clarification of these issues.

5. Claim Rejections - 35 USC § 112, first paragraph – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 134-146 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

B. Even if claims 134-146 possessed utility under 35 USC 101, these claims would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for a method of identifying modulators of apoptosis by screening compounds using a p75 neurotropin receptor and the NADE of SEQ ID NO:12 or 13 of the present invention, does not reasonably provide enablement for this method using p75 and any other p75-associated cell death executor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to Applicant claiming a method of identifying modulators of apoptosis by screening compounds using a p75 neurotropin receptor and any cell death executors. Applicant has only provided guidance and working examples of the interaction of the p75 neurotropin receptor with one particular cell death executor, the NADE of SEQ ID NO:12 or 13 (pages 55-57 of the specification and Figures 2 and 3). Applicant has provided no other guidance or working examples of any other p75 neurotropin receptor/cell death executor complexes, nor that formation of any of these other complexes leads to apoptosis. The NADE of SEQ ID NO:12 or 13 of the present invention, which is the only enabled cell death executor of the present invention, has a specific amino acid sequence. "**NADE" proteins**," or "**cell death executor**" proteins other than SEQ ID NO:12 or 13 would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein

of SEQ ID NO:12 or 13. Applicant, respectfully, has provided no guidance or working examples of what amino acids are critical for cell death executor function, only speculation based on homology to known proteins, none of which have been shown to interact with p75 (Figure 1). Therefore, one of ordinary skill in the art would not know how to make a functional NADE, or other cell death executor, other than that of SEQ ID NO:12 or 13 of the present invention. Given only guidance of this one p75/NADE complex, it would not be predictable to one of ordinary skill in the art how to make any other p75/cell death executor complexes other than that of p75 and the specific NADE of the invention.

Therefore, in summary, the breadth of the claims is excessive with regard to Applicant claiming methods of identifying modulators of apoptosis by screening compounds using a p75 neurotropin receptor and NADE or cell death executors other than that of SEQ ID NO:12 or 13 of the present invention. Applicant has provided no guidance and working examples of the use of any other cell death executor other than that of SEQ ID NO:12 or 13. Given this lack of guidance and working examples, it would not be predictable to the artisan how to make a cell death executor other than that of SEQ ID NO:12 or 13. Therefore, the Examiner has concluded that undue experimentation is required to practice the invention as claimed.

Both SEQ ID NO:12 and 13 are recited in this rejection since, as recited in paragraph C of this Action, it is not clear which SEQ ID NO, if either, is the one used in the Examples of the present invention. If neither SEQ ID NO:12, nor 13 is not the NADE used in the Examples in the present application, the Applicant is required to clarify this issue, or Applicant's response will be held non-responsive.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 134-146 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

"**NADE" proteins**," or "**cell death executor**" proteins other than SEQ ID NO:13 would have one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:13. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The

specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:13 alone is insufficient to describe the genus.

The specification provides a written description of only a small number of these nucleic acid constructs (SEQ ID NO:13). No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues which would structurally characterize the genus of nucleic acids encoding the genus of NADE or cell death executor proteins claimed, because it is unknown and not described what structurally constitutes any different proteins encoding NADE or cell death executors, or NADE and cell death executor proteins from any different species, which are further not described; thereby not meeting the written description requirement under 35 USC 112, first paragraph. Therefore, one of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 112, first paragraph – new matter

A. On page 14 of the Office Action dated 3/27/02, the previous Examiner stated under 35 USC 102, paragraph 13, for example, that the specification appears to contain new matter because the nucleic acid originally filed and the nucleic acids presented in the sequence listing are not the same. Applicants are requested to address this issue.

8. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 134-146 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of the term "NADE" and "cell death executor" is not known. The word

"NADE" is an acronym and both this term and the phrase "cell death executor" are arbitrary terms given to a potential group of proteins which the metes and bounds of have not been specifically defined in the specification. If these terms have been precisely defined in the specification, Applicant is required to point out exactly where these definitions are found. Respectfully, merely a simple definition of these terms will not overcome this rejection. For example, "a protein which interacts, or binds to p75 and which is involved with apoptosis" would not be acceptable since many proteins associate with, or bind to p75 and, since p75 itself is known to be involved with apoptosis, this definition would not specifically and clearly define the "NADE" or "cell death executor" class.

9. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
April 21, 2003

ROBERT LANDSMAN
PATENT EXAMINER